

**IN THE CLAIMS:**

Please amend claims 1-35 as shown below in the detailed listing of all claims which are, or were, in this application:

1. (Currently amended) A method for preparing a sol-gel derived  $\text{SiO}_2$  monolith, ~~preferably with a minimum diameter of  $\geq 0.5$  mm,~~ coating, ~~preferably with a thickness of  $< 0.5$  mm,~~ or particle, ~~preferably with a maximum diameter of  $\leq 100$   $\mu\text{m}$ , with having~~ a very fast bioresorption rate, said  $\text{SiO}_2$  optionally comprising a specific percentage or percentages of a biologically active agent or agents other than the  $\text{SiO}_2$  itself with or without protective agent or agents for said biologically active agent or agents, wherein said method comprising preparing a sol-gel derived  $\text{SiO}_2$  ~~is prepared~~ from a sol comprising water, an alkoxide or inorganic silicate and a lower alcohol~~[[~~, i.e. an alcohol~~]]~~ with  $\leq 4$  carbons, using a mineral acid or a base as a catalyst, ~~preferably a mineral acid,~~ and aging said sol ~~is aged and dried characterised in that drying~~ said sol, wherein

a) in the sol the starting

i) pH is from 0.05 to 2.5, ~~preferably 1.5 to 2.5, most preferably 2.0,~~

ii) molar ratio of water to the alkoxide or inorganic silicate is 0.5 to 2.5, ~~preferably 1.5 to 2.5,~~

iii) molar ratio of alcohol to the alkoxide or inorganic silicate is  $\geq 0.5$ , ~~preferably  $\geq 1.0$~~ ; and

b) either,

i) the sol is, without induced changes of sol composition,

- let to gel spontaneously at a temperature of  $\leq 25$  °C or an elevated temperature of 65 °C to 90 °C, ~~preferably at an elevated temperature of 65 °C to 90 °C, or~~
- gelation of the sol is done by forced drying of the sol, or

ii) a change or changes of sol composition are induced after sol ageing but before gel formation, said change or changes of sol composition optionally comprising addition of said biologically active agent or agents with or without said protective agent or agents, and

the ratio  $t/t_{gel}$  is  $\geq 0.005$ , ~~preferably  $\geq 0.1$ , most preferably  $\geq 0.9$~~ , wherein

$t$  is the ageing time of the sol, i.e. time from preparation of said sol to the induced changes, and

$t_{gel}$  is the time point where the sol would have turned to a gel without the induced changes; and forced drying of the sol is carried out or initiated within a time of  $\leq$  30 minutes[], preferably  $\leq$  15 minutes, most preferably  $\leq$  5 minutes, from said induced change or changes[].

2. (Currently amended) A method for adjusting the bioresorption rate of sol-gel derived  $\text{SiO}_2$  monolith, ~~preferably with a minimum diameter of  $\geq$  0.5 mm, coating, preferably with a thickness of  $\leq$  0.5 mm, or particle, preferably with a maximum diameter of  $\leq$  100 mm, optionally comprising a specific percentage or percentages of a biologically active agent or agents other than the  $\text{SiO}_2$  itself with or without protective agent or agents for said biologically active agent or agents, characterised in that wherein~~

A) a  $\text{SiO}_2$  with a very fast bioresorption rate is obtained according to the method of preparing a  $\text{SiO}_2$  of claim 1; and

B) a  $\text{SiO}_2$  with a slower bioresorption rate than the very fast bioresorption rate is obtained by correlating a desired biodegradability of a  $\text{SiO}_2$  with changes a), b) and/or c) to said method of preparing a  $\text{SiO}_2$ , wherein

a) comprises deviating in the sol any of the starting values:

- i) pH,
- ii) molar ratio of water to the alkoxide or inorganic silicate, and/or
- iii) molar ratio of alcohol to the alkoxide or inorganic silicate;

from the values defined in a) i) - iii) of said method of preparing a  $\text{SiO}_2$ ;

b) comprises carrying out induced changes by addition of a component or components, including optional addition of the biologically active agent or agents with or without said protective agent or agents, said changes affecting any of the values i) - iii) of a) of said method of preparing a  $\text{SiO}_2$  or a) above if applied by

- i) not carrying out forced drying, or
- ii) carrying out or initiating forced drying of the sol later than defined in b) ii) of said method of preparing a  $\text{SiO}_2$ ; and

c) comprises deviating the temperature for letting the sol gel spontaneously from the values defined in b) i) of said method of preparing a  $\text{SiO}_2$ ; and a method for preparing the  $\text{SiO}_2$  with said changes to the method correlating with the desired biodegradability is carried out for obtaining the  $\text{SiO}_2$  with the desired slower biodegradability.

3. (Currently amended) The method according to claim 2 ~~characterised in that~~ wherein an alkoxide, ~~preferably tetraethoxysilane (TEOS), is used for preparing to prepare~~ the sol-gel derived  $\text{SiO}_2$ .

4. (Currently amended) The method according to claim 2 ~~characterised in that~~ ~~that~~ wherein an inorganic silicate, ~~preferably sodium or potassium silicate, is used for preparing to~~ prepare the sol-gel derived  $\text{SiO}_2$ .

5. (Currently amended) The method according to claim 2 ~~characterised in that~~ wherein the lower alcohol is ethanol.

6. (Currently amended) The method according to claim 2  
**characterised** in that wherein the induced change is selected from the group consisting of adding water, adding the alkoxide or inorganic silicate, adding the alcohol, adjusting pH by adding an acid or base, ~~preferably the acid or base used as the catalyst,~~ adding the optional bioactive agent or agents with or without protective agent or agents for said biologically active agent or agents affecting any of the values i) - iii) of a) of said method of preparing a SiO<sub>2</sub> or a) of said method of adjusting the bioresorption of sol-gel derived SiO<sub>2</sub> if applied, and any combination thereof.

7. (Currently amended) The method according to claim 2  
**characterised** in that wherein ~~drying of~~ the sol is ~~drying~~ dried by a member of the group consisting of ambient heat, vacuum drying, electromagnetic drying, acoustic drying, spray-drying or and freeze-drying, ~~preferably spray-drying or freeze-drying.~~

8. (Currently amended) The method according to claim 2  
**characterised** in that wherein the sol is dried by forced drying of

~~the sol is carried out, preferably by spray-drying or freeze-drying.~~

9. (Currently amended) The method according to claim 8  
**characterised in that** wherein forced drying is freeze-drying initiated by freezing the sol.

10. (Currently amended) The method according to claim 8  
**characterised in that** wherein the temperature of the sol is  
 $\leq +90^{\circ}\text{C}$ [], preferably  $\leq +50^{\circ}\text{C}$ , most preferably  $\leq +40^{\circ}\text{C}$ ].

11. (Currently amended) The method according to claim 2  
**characterised in that** wherein the gel is dried.

12. (Currently amended) The method according to claim 11  
**characterised in that** wherein ~~drying of~~ the gel is ~~drying~~ dried by  
a member of the group consisting of ambient heat, vacuum drying,  
electromagnetic drying, acoustic drying, spray-drying **or and**  
freeze-drying, ~~preferably ambient heat or freeze-drying.~~

13. (Currently amended) The method according to claim 11  
~~characterised in that wherein~~ the gel is dried at a temperature of  
 $\leq 700^{\circ}\text{C}$ , ~~preferably~~  $\leq 50^{\circ}\text{C}$ , and ~~most preferably~~  $\leq 40^{\circ}\text{C}$ .

14. (Currently amended) The method according to claim 2  
~~characterised in that wherein~~ a value to be deviated to obtain a  
slower bioresorption rate is the ratio of water to the alkoxide or  
inorganic silicate, and the more the ratio of water to alkoxide or  
inorganic silicate is deviated to be higher or lower the slower the  
bioresorption rate obtained.

15. (Currently amended) The method according claim 2 ~~characterised~~  
~~in that wherein~~ a value to be deviated to obtain a slower  
bioresorption rate is the ratio of alcohol to the alkoxide or  
inorganic silicate, and the more the ratio is deviated to be higher  
or lower the slower the bioresorption rate obtained.

16. (Currently amended) The method according to claim 2  
~~characterised in that wherein~~ a value to be deviated to obtain a  
slower bioresorption rate is the pH, and the more the pH is

deviated to be higher or lower the slower the bioresorption rate obtained.

17. (Currently amended) The method according to claim 2  
~~characterised in that~~ wherein a biologically active agent or agents is added to the sol before gel formation.

18. (Currently amended) The method according to claim 2  
~~characterised in that~~ wherein any of the values pH, molar ratio of water to the alkoxide or inorganic silicate, and/or molar ratio of alcohol to the alkoxide or inorganic silicate is changed to deviate from the ranges defined in said method of preparing a SiO<sub>2</sub>, a) ic) - iii), after sol ageing but before gel formation and/or optional addition of said biologically active agent or agents, and within ≤ 30 minutes[[, preferably ≤ 15 minutes and most preferably ≤ 5 minutes]] from the change forced drying of the sol is carried out or initiated.

19. (Currently amended) The method according to claim 2  
~~characterised in that~~ wherein the biologically active agent or agents is selected from the group consisting of a drug, peptide,

protein, hormone, growth factor, enzyme, polysaccharide, living or dead cells or viruses or parts thereof, plasmids, polynucleotides, water soluble ions, salts and any combination thereof.

20. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, **characterised** in **that** wherein

- a) the SiO<sub>2</sub> is a monolith[], preferably with a minimum diameter of  $\geq 0.5\text{ mm}$ ],
- b) the SiO<sub>2</sub> comprises no biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in a TRIS buffer at a temperature of +37 °C and pH 7.4 is  $\geq 0.04\text{ wt-\%}/\text{h}$ [], preferably  $\geq 0.07\text{ wt-\%}/\text{h}$  and more preferably  $\geq 0.15\text{ wt-\%}/\text{h}$ ].

21. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, **characterised** in **that** wherein

- a) the SiO<sub>2</sub> is a monolith[], preferably with a minimum diameter of  $\geq 0.5\text{ mm}$ ],

- b) the SiO<sub>2</sub> comprises at least one biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in a TRIS buffer at a temperature of +37 °C and pH 7.4 is ≥ 0.35 wt-%/h.

22. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, ~~characterised in that wherein~~

- a) the SiO<sub>2</sub> is a coating[], preferably with a thickness of < 0.5 mm[],
- b) the SiO<sub>2</sub> comprises no biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in TRIS buffer at a temperature of +37 °C and pH 7.4 is ≥ 0.04 wt-%/h[], preferably ≥ 0.07 wt-%/h and more preferably ≥ 0.15 wt-%/h[].

23. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, ~~characterised in that wherein~~

- a) the SiO<sub>2</sub> is a coating[], preferably with a thickness of < 0.5 mm[],

- b) the SiO<sub>2</sub> comprises at least one biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in TRIS buffer at a temperature of +37 °C and pH 7.4 is ≥ 0.04 wt-%/h[], preferably ≥ 0.07 wt-%/h and more preferably ≥ 0.15 wt-%/h[].

24. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2 ~~characterised in that~~ wherein

- a) the SiO<sub>2</sub> is a particle[], preferably with a maximum diameter of ≤ 100 μm[],
- b) the SiO<sub>2</sub> comprises no biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in TRIS buffer at a temperature of +37 °C and pH 7.4 is ≥ 0.04 wt-%/h[], preferably ≥ 0.07 wt-%/h and more preferably ≥ 0.15 wt-%/h[].

25. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2 ~~characterised in that~~ wherein

- a) the SiO<sub>2</sub> is a particle[], preferably with a maximum diameter of ≤ 100 µm],
- b) the SiO<sub>2</sub> comprises at least one biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in TRIS buffer at a temperature of +37 °C and pH 7.4 is ≥ 0.5 wt-%/h.

26. (Currently amended) The SiO<sub>2</sub> according to claim 20,  
~~characterised in that~~ wherein the dissolution rate of the SiO<sub>2</sub> is  
≥ 0.30 wt-%/h.

27. (Currently amended) The SiO<sub>2</sub> according to claim 21,  
~~characterised in that~~ wherein the dissolution rate of the SiO<sub>2</sub> is  
≥ 0.5 wt-%/h [preferably ≥ 1.0 wt-%/h, more preferably  
≥ 2.0 wt-%/h and most preferably ≥ 4.0 wt-%/h].

28. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, ~~characterised in that~~ wherein

- a) the SiO<sub>2</sub> is a monolith[], preferably with a minimum diameter of ≥ 0.5 mm],

b) the SiO<sub>2</sub> comprises no biologically active agent other than the SiO<sub>2</sub> itself, and

c) the dissolution rate of the SiO<sub>2</sub> in a TRIS buffer at a temperature of +37 °C and pH 7.4 is from 0.001 to 0.15 wt-%/h[], preferably from 0.002 to 0.07 wt-%/h, and more preferably from 0.006 to 0.05 wt-%/h].

29. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2, ~~characterised in that~~ wherein

a) the SiO<sub>2</sub> is a monolith[], preferably with a minimum diameter of ≥ 0.5 mm],

b) the SiO<sub>2</sub> comprises at least one biologically active agent other than the SiO<sub>2</sub> itself, and

c) the dissolution rate of the SiO<sub>2</sub> in a TRIS buffer at a temperature of +37 °C and pH 7.4 is from 0.001 to 0.06 wt-%/h [], preferably from 0.002 to 0.05 wt-%/h, and from 0.006 to 0.025 wt-%/h].

30. (Currently amended) The SiO<sub>2</sub> according to claim 22 ~~characterised in~~ wherein the dissolution rate of the SiO<sub>2</sub> in

TRIS buffer at a temperature of +37 °C and pH 7.4 is from 0.001 to 0.15 wt-%/h[], preferably from 0.002 to 0.07 wt-%/h, and more preferably from 0.006 to 0.05 wt-%/h].

31. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2 ~~characterised~~ in that wherein

- a) the SiO<sub>2</sub> is a particle[], preferably with a maximum diameter of ≤ 100 μm],
- b) the SiO<sub>2</sub> comprises no biologically active agent other than the SiO<sub>2</sub> itself, and
- c) the dissolution rate of the SiO<sub>2</sub> in TRIS buffer at a temperature of +37 °C and pH 7.4 is from 0.001 to 0.008[], and preferably from 0.002 to 0.003 wt-%/h].

32. (Currently amended) A bioresorbable sol-gel derived SiO<sub>2</sub>, obtainable according to the method of claim 2 ~~characterised~~ in that wherein

- a) the SiO<sub>2</sub> is a particle[], preferably with a maximum diameter of ≤ 100 μm],

b) the  $\text{SiO}_2$  comprises at least one biologically active agent other than the  $\text{SiO}_2$  itself, and

c) the dissolution rate of the  $\text{SiO}_2$  in TRIS buffer at a temperature of +37 °C and pH 7.4 is from 0.001 to 0.10 wt-%/h [[, preferably from 0.002 to 0.07 wt-%/h, and more preferably from 0.006 to 0.05 wt-%/h]] .

33. (Currently amended) A bioresorbable sol-gel derived  $\text{SiO}_2$  monolith, ~~preferably with a minimum diameter of  $\geq 0.5$  mm~~, coating, ~~preferably with a thickness of  $< 0.5$  mm~~, or particle, ~~preferably with a maximum diameter of  $\leq 100$   $\mu\text{m}$~~ , obtainable according to the method of claim 2, wherein said  $\text{SiO}_2$  comprises a biologically active agent other than the  $\text{SiO}_2$  itself and said biologically active agent is a peptide, protein or cell, **characterised** in that wherein the dissolution rate of the  $\text{SiO}_2$  in TRIS buffer at a temperature of +37 °C and pH 7.4 is  $\geq 0.04$  wt-%/h[[, preferably  $\geq 0.07$  wt-%/h and more preferably  $\geq 0.15$  wt-%/h]] .

34. (Currently amended) A bioresorbable sol-gel derived  $\text{SiO}_2$  monolith, ~~preferably with a minimum diameter of  $\geq 0.5$  mm~~, coating, ~~preferably with a thickness of  $< 0.5$  mm~~, or particle, ~~preferably~~

~~with a maximum diameter of  $\leq 100 \mu\text{m}$ , obtainable according to the method of claim 2, wherein said  $\text{SiO}_2$  comprises a biologically active agent other than the  $\text{SiO}_2$  itself and said biologically active agent is a peptide, protein or cell, characterised in that wherein the dissolution rate of the  $\text{SiO}_2$  is  $\geq 0.5 \text{ wt-\%}/\text{h}$  and preferably  $\geq 4.0 \text{ wt-\%}/\text{h}$ .~~

35. (Currently amended) A bioresorbable sol-gel derived  $\text{SiO}_2$  monolith, ~~preferably with a minimum diameter of  $\geq 0.5 \text{ mm}$ , coating, preferably with a thickness of  $< 0.5 \text{ mm}$ , or particle, preferably with a maximum diameter of  $\leq 100 \mu\text{m}$ , obtainable according to the method of claim 2, wherein said  $\text{SiO}_2$  comprises a biologically active agent other than the  $\text{SiO}_2$  itself and said biologically active agent is a peptide, protein or cell, characterised in that wherein the dissolution rate of the  $\text{SiO}_2$  in TRIS buffer at a temperature of  $+37^\circ\text{C}$  and pH 7.4 is from 0.001 to 0.15  $\text{wt-\%}/\text{h}[[$ , preferably from 0.002 to 0.07  $\text{wt-\%}/\text{h}$ , and more preferably from 0.006 to 0.05  $\text{wt-\%}/\text{h}]]$ .~~

36. (Previously presented) Use of a bioresorbable sol-gel derived  $\text{SiO}_2$  according to claim 20 for administering a biologically active

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RESPONSE TO RESTRICTION REQUIREMENT

**PATENT**

agent to a human or animal body, wherein said use comprises administering selected from the group consisting of oral, buccal, rectal, parenteral, pulmonary, nasal, ocular, intrauterine, vaginal, urethral, topical, transdermal and surgically implantable administering.

37. (Previously presented) Use of a bioresorbable sol-gel derived SiO<sub>2</sub> according to claim 20 for administering a biologically active agent to a plant.